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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/853,409	05/11/2001	Kevin P. Anderson	ISPH-0569	7066

26259 7590 10/21/2003

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EXAMINER	
GUZO, DAVID	

ART UNIT	PAPER NUMBER
1636	17

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/853,409	Applicant(s) ANDERSON ET AL.	
	Examiner David Guzo	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 23-27 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 23-27 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). 16 .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Detailed Action

The non-responsive letter mailed 07/03/03 is vacated. A non-final rejection on all pending claims follows.

35 USC 102 Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 23 is rejected under 35 U.S.C. 102(b) as being anticipated by Smith et al. or Storey et al.

Applicants claim a composition comprising an oligonucleotide 5 to 50 nucleotides in length which is complementary to at least a portion of a HCV genomic or messenger mRNA in a form suitable for subcutaneous administration. It is noted that applicants do not define how a composition, or a oligonucleotide, suitable for subcutaneous administration would differ from any pharmaceutically acceptable composition, or oligonucleotide, suitable for *in vivo* administration by any method (i.e. intravenous, intramuscular, etc.); therefore, an oligonucleotide (of the recited size range) complementary to at least a portion of the HCV genome or HCV mRNA in any pharmaceutically acceptable carrier will be considered, absent evidence to the contrary, to anticipate the claimed invention.

Smith et al. (PNAS, 1986, Vol. 83, pp. 2787-2791, see whole article, particularly the Abstract and first two paragraphs of the "Materials and Methods" section on p. 2787) recites the antisense oligonucleotide 5'-TpCCTCCTG-3', which contains a region complementary to a portion of the HCV genome (the sequence CAGGA at position 115 to 119 recited in instant SEQ ID NO:37). Smith et al. also recites a composition comprising the oligonucleotide in phosphate buffered saline, which is a pharmaceutically acceptable carrier and would, absent evidence to the contrary, be suitable for subcutaneous administration.

Storey et al. (Nucleic Acids Res., August, 1991, Vol. 19, No. 15, pp. 4109-4114, see whole article, particularly the last paragraph on p. 4109 and Fig. 1) recites an antisense oligonucleotide (GCAGTTCTCTTTTGGTGCATAA) which contains a sequence (TTTGGT) complementary to a portion of the HCV genomic RNA (the sequence ACCAAA at position 371-376 of instant SEQ ID NO:37). Storey et al. also recites a composition comprising the oligonucleotide in distilled water, which is a pharmaceutically acceptable carrier and would, absent evidence to the contrary, be suitable for subcutaneous administration.

Double Patenting Rejections

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 23-27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,608,191. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. First, it is again noted that applicants do not do not define, in the instant specification, how a composition comprising an antisense oligonucleotide in a form suitable for subcutaneous administration differs from any other composition suitable for *in vivo* use. Therefore, it must be considered, absent evidence to the contrary, that the claims read on a composition comprising the recited oligonucleotides with a pharmaceutically acceptable carrier. Also, the SEQ ID NO:6 in the '191 patent is the same oligonucleotide as SEQ ID NO:6 recited in the instant claims.

The instant composition and method claims (23-27) are obvious in view of claim 1 of the '191 patent because the antisense oligonucleotide (SEQ ID NO:6) recited in the '191 patent and the instant application is complementary to the translation initiation start site of the HCV genome and is designed to be used to inhibit expression of the HCV genome in cells in patients. Therefore, the ordinary skilled artisan would have been motivated to incorporate the oligonucleotide recited in the '191 patent (SEQ ID NO:6) into a pharmaceutically acceptable composition suitable for *in vivo* use (subcutaneous

administration) and use the recited oligonucleotide to inhibit HCV expression because the antisense oligonucleotide targets an essential region for HCV gene expression and is designed to be used to inhibit HCV gene expression in patients. It would have been obvious for the ordinary skilled artisan to do this because the recited antisense oligonucleotide is targeted against a region critical in HCV gene expression and could be used to treat patients suffering from HCV infection. Given the claim in the '191 patent and the level of skill of the ordinary skilled artisan at the time the invention was made, it must be assumed that the skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 23-27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 7 of U.S. Patent No. 6,423,489. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. Initially, it is noted that SEQ ID NO:73 recited in claim 1 of the '489 patent is the same as SEQ ID NO:6 in the instant application. Also, claim 7 of the '489 patent encompasses a method for inhibiting the activity of HCV in cells *in vitro* and *in vivo*. It must be considered that a method for inhibiting HCV activity in cells *in vivo* would involve administration of the oligonucleotide in a pharmaceutically acceptable composition.

The ordinary skilled artisan, seeking to administer an antisense HCV oligonucleotide to patients for inhibition of HCV activity would have been motivated to incorporate the oligonucleotide in a pharmaceutically acceptable carrier (for

administration *in vivo* by standard routes such as by subcutaneous administration) because administration of compounds such as oligonucleotides to humans must be in a safe form such as a pharmaceutically acceptable composition. It would have been obvious for the ordinary skilled artisan to use the recited oligonucleotides to inhibit HCV gene expression (and thereby treat an HCV associated disease) in a human because the claims in the '489 patent recite use of antisense oligonucleotides to inhibit HCV activity in cells *in vitro* and *in vivo*.

Claims 23-27 are directed to an invention not patentably distinct from claim 1 of commonly assigned 6,608,191 and claims 1 and 7 of commonly assigned 6,423,489. Specifically, the claims are not patentably distinct for the reasons recited in the above obviousness type double patenting rejections.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned 6,423,489 and 6,608,191, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the

prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

35 USC 112, 2nd Paragraph Rejections

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23-27 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 (and dependent claims) is vague in that applicants recite a composition comprising an oligonucleotide and further recite "in a form suitable for subcutaneous administration.". It is unclear if the phrase "in a form suitable for subcutaneous administration" relates only to the oligonucleotide component or to the composition comprising the oligonucleotide.

No Claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (703) 305-19989. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

DAVID GUZO
PRIMARY EXAMINER

David Guzo
October 10, 2003